ACC.12
61st Annual Scientific Session & Expo
ACC-i2 with TCT innovation in intervention

E457
JACC March 27, 2012
Volume 59, Issue 13

Acute Coronary Syndromes

HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS ATTENUATE THE LEFT VENTRICULAR REMODELING AFTER ACUTE MYOCARDIAL INFARCTION IN RATS VIA A REGULATION OF MATRIX METALLOPROTEINASES/TISSUE INHIBITOR OF METALLOPROTEINASES BALANCE BY ENDOTHELIAL NITRIC OXIDE SYNTHASE

ACC Oral Contributions
McCormick Place North, N227b
Sunday, March 25, 2012, 11:00 a.m.-11:15 a.m.

Session Title: Improving Outcomes in ACS. Insights from Basic Science and Preclinical Research.
Abstract Category: 6. Acute Coronary Syndromes: Basic
Presentation Number: 917-4

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Background: The establishment of various stem cell sources that can effectively treat a variety of diseases, that are free from ethical obstacles, and that are not difficult to isolate difficult is extremely crucial in stem cell therapy. We therefore elucidated the therapeutic potential of human umbilical vein endothelial cells (HUVECs) as a new, appropriate stem cell source for ameliorating progressive heart failure in an acute myocardial infarction (MI) rat model.

Methods and Results: In an acute MI rat model, HUVECs, which had been injected directly into the infarct border zone, effectively attenuated left ventricular systolic dysfunction and remodeling compared with the control group [left ventricular end-diastolic dimension (mm); in the control (n = 6) vs. HUVEC (n = 6) group, respectively: 11.23±0.57 vs. 10.04±0.89, $p<0.05$; left ventricular end-systolic dimension (mm): 9.33±0.45 vs. 8.34 ±0.65, $p<0.05$; and left ventricular end-diastolic pressure (mmHg); 18.41±6.08 vs. 8.16±5.55, $p<0.05$]. In the same tissue, a population of injected HUVECs was observed that expressed both cardiac maker (cTnI) and constituted gap junction (connexin 43) with adjacent rat cardiomyocytes. However, many HUVECs existed without differentiation into specific cell type, and endothelial nitric oxide synthase (eNOS) expression cells were detected in the infarct myocardium. In vivo zymography analysis showed that HUVECs decreased the ratio of matrix metalloproteinase (MMP)-2 and MMP-9 to tissue inhibitor of metalloproteinase (TIMP)-1 and TIMP-3. In immunohistochemistry, decreased MMP-2 and increased TIMP-1 and TIMP-3 expression in infarct myocardium were observed at 48 hours after cell injection. These effects were inhibited by L-NAME (an eNOS inhibitor, 10 mg/kg). NOS inhibition decreased the protein expression of TIMP-1 and TIMP-3 but did not change the protein expression of MMP-2 and MMP-9.

Conclusions: Our results show that HUVECs can be considered a new cell candidate for ischemic heart failure after acute MI and that their mechanism of action is through the inactivation of MMPs via eNOS.